

Regulatory CD19⁺CD24^{hi}CD38^{hi} B cells are decreased in patients with coronary atherosclerosis and have impaired interleukin-10 production in response to CpG

I. E. Dumitriu, P. Baruah, S. Dinkla, J. Bullenkamp and J. C. Kaski

Background/Introduction: B-lymphocytes have critical roles in the inflammatory process that drives atherosclerosis. In animal models, conventional B2 B cells promote atherosclerosis, whilst innate B1a B cells are protective. B cells with regulatory function (Bregs) have been identified in animals and humans and have been implicated in the pathogenesis of autoimmunity. Whether Bregs have a role in human atherosclerosis is currently unknown.

Purpose: Our aim was to characterise the frequency, phenotype and function of Bregs in atherosclerosis patients.

Methods: CD19⁺CD24^{hi}CD38^{hi} Bregs were quantified in patients with atherosclerosis (myocardial infarction (MI), n=60; stable angina, SA, n=40), and in healthy subjects (n=30) using flow cytometry. Interleukin-10 (IL-10) production was quantified by intracellular staining.

Results: The percentage and absolute number of circulating Bregs were markedly reduced in MI and SA patients compared to healthy subjects. No differences were noted in total, mature or memory B cells, suggesting a specific depletion of the Breg cell subset. Bregs from MI and SA patients produced significantly less IL-10 in response to CpG compared to Bregs from healthy subjects, whilst stimulation with CD40L elicited similar levels of IL-10 in all study groups. Moreover, IL-10 production by mature and memory B cells was not impaired in MI and SA patients. Molecular mechanisms that underlie defects in Bregs in patients with atherosclerosis are being characterised.

Conclusions: Our data show for the first time that patients with atherosclerosis harbour marked numerical and functional defects in Breg cells that may tip the balance in favour of pro-inflammatory B and T lymphocytes. A better understanding of these defects may reveal novel targets for therapies to tackle inflammation in atherosclerosis.